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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,297	HALL ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2006* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,47 and 62-84* is/are pending in the application.

4a) Of the above claim(s) *64,69,70 and 74-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,47,62,63,65-68,71-73 and 78-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on March 27, 2006 has been entered. The claims pending in this application are claims 35, 47, and 62-84 wherein claims 64, 69, 70, and 74-77 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on March 27, 2006. Claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 will be examined.

Election of Species

Response to Arguments

In page 7, first paragraph of applicant's remarks, applicant argues that "[T]he withdrawal of Claims 74-77 is improper as Claim 73 reads on these embodiments. Single embodiments (as detailed in the Amendment and Response filed on October 3, 2005) can have all of the limitations of Claims 73-75, and the limitations of one of these claims do not preclude the limitations of the others from being found in a single embodiment – *i.e.,* they are not mutually exclusive".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that species 74-77 will be examined together. First, since claim 73 requires that said first nucleic acid molecule is in concentration excess compared to said target nucleic acid, claim 74 requires that said second nucleic acid molecule is in concentration excess compared to said target nucleic acid, and claim 75 requires that said first nucleic acid molecule is in concentration

excess compared to said duplex, and these species are directed to different embodiments and species 6, 7, and 8 are mutually exclusive because each claims (claims 73-75) has a specific limitation which is not found in other claims. Therefore, the requirement is still deemed proper.

Claim Objections

2. Claim 35 is objected to because of the following informality: "cleaved second probe" in steps b) and c) should be "the cleaved second probe".

3. Claim 47 is objected to because of the following informality: "cleaved second probe" should be "the cleaved second probe".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 35 is rejected as vague and indefinite in view of step a) because it is unclear how a second cleavage structure comprising a second probe oligonucleotide can be formed without a step that hybridizes the second probe oligonucleotide to said cleaved unpaired region since "wherein" phrases in step a) can not be considered as a method step. Please clarify.

Response to Arguments

In page 8, four paragraph bridging to page 9, third paragraph of applicant's remarks, applicant argues that "[T]he Examiner has not explained why the invention should be limited to embodiments in which the probe oligonucleotide hybridizes to the cleaved unpaired region. Applicants submit that it is not limited to this embodiment. For the reasons described above, Applicants submit that the specification clearly teaches how cleavage structures, including second cleavage structures, are formed, and further submits that the claims provide all of the details needed to particularly point out and distinctly claim the subject matter which the Applicants regard as their invention. Applicants respectfully request that these rejections be removed" because, as shown in Figure 96, "the cleaved unpaired region and the second probe do not hybridize to each other".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the rejection. Since the claim does not contain target 2 which hybridizes to both the second probe oligonucleotide and said cleaved unpaired region as shown in Figure 96, without a step that hybridizes the second probe oligonucleotide to said cleaved unpaired region, a second cleavage structure comprising said cleaved unpaired region and a second probe oligonucleotide cannot be formed so that a cleaved second probe cannot be produced and steps b) and c) of the claim cannot be performed.

7. Claim 62 is rejected as vague and indefinite in view of step b) because it is unclear how a second cleavage structure comprising a probe oligonucleotide can be formed without a step that hybridizes the probe oligonucleotide to said non-target cleaved product. Please clarify.

Response to Arguments

In page 9, last paragraph bridging to page 10, last paragraph of applicant's remarks, applicant argues that "[T]he Examiner has not explained why the invention should be limited to embodiments in which the probe oligonucleotide hybridizes to the cleaved unpaired region. Applicants submit that it is not limited to this embodiment. For the reasons described above, Applicants submit that the specification clearly teaches how cleavage structures, including second cleavage structures, are formed, and further submits that the claims provide all of the details needed to particularly point out and distinctly claim the subject matter which the Applicants regard as their invention. Applicants respectfully request that these rejections be removed" because, as shown in Figure 96, "the cleaved unpaired region and the second probe do not hybridize to each other".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the rejection. Since the claim does not contain target 2 which hybridizes to both the probe oligonucleotide to said non-target cleaved product as shown in Figure 96, without a step that hybridizes the probe oligonucleotide to said non-target cleaved product, a second cleavage structure comprising said non-target cleaved product and the probe oligonucleotide cannot be formed so that a cleaved probe cannot be produced and steps c) and d) of the claim cannot be performed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 35, 47, 62, 63, 66, 71, and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodman et al., (US Patent No. 4,994,368, published on February 19, 1991).

Regarding claims 35 and 47, Goodman *et al.,* teach a method of producing multiple copies of a primary polynucleotide sequence as the result of the presence of a target polynucleotide sequence located at the 3' terminus of a polynucleotide, which comprises: (a) forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences; (b) cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences; (c) dissociating said fragments, wherein said fragments comprise said primary polynucleotide sequence; (d) hybridizing said fragments with said single stranded pattern polynucleotide; (e) forming in the presence of said nucleoside triphosphates and said template dependent polynucleotide polymerase an extension of said fragments hybridized with said single stranded pattern polynucleotide; and (f) repeating steps (b)-(e) above wherein steps (b)-(e) are conducted simultaneously or wholly or partially sequentially (see claim 18, column 30 and Figures 1-4). Since Goodman *et al.,* teach forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide

sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences and cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences (see claim 18, column 30 and Figures 1-4), Goodman *et al.,* disclose contacting a target polynucleotide (ie., target polynucleotide sequence taught by Goodman *et al.,*) having a first portion and a second portion immediately contiguous to one another with: i) an invader oligonucleotide (i.e., one site specific cleavage sequence), at least a part of which is capable of specifically hybridizing to the first portion of the target polynucleotide; ii) a first probe oligonucleotide (i.e., another site specific cleavage sequence) comprising a first region that is capable of specifically hybridizing to the second portion of the target polynucleotide and an unpaired region located adjacent to the first region; and iii) a reagent that is capable of cleaving the unpaired region of the probe oligonucleotide (i.e, means for specifically cleaving said cleavable polynucleotide sequences) when the probe oligonucleotide is hybridized to the second portion of the target polynucleotide and the invader oligonucleotide is hybridized to the first portion of the polynucleotide as recited in claim 35. Since Goodman *et al.,* teach cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences, dissociating said fragments wherein said fragments comprise said primary polynucleotide sequence, hybridizing said fragments with said single stranded pattern polynucleotide, forming

in the presence of said nucleoside triphosphates and said template dependent polynucleotide polymerase an extension of said fragments hybridized with said single stranded pattern polynucleotide, and repeating steps (b)-(e) above wherein steps (b)-(e) are conducted simultaneously or wholly or partially sequentially (see above) wherein said fragments are labeled with a fluorescence after cleavage (see claims 11-17 in claims 29 and 30, columns 14 and 15, and Figure 2), Goodman *et al.,* disclose under conditions wherein said first probe oligonucleotide is cleaved to produce said cleaved unpaired region (ie., cleaved unpaired region includes both unpaired region and some paired region, see cleaved fragments (duplex 8) taught by Goodman *et al.,* in Figure 2), wherein a second cleavage structure (ie., duplex 9 taught by Goodman *et al.,* in Figure 2) cleavable by said reagent is formed, said second cleavage structure comprising said cleaved unpaired region and a second probe oligonucleotide, and wherein said second cleavage structure is cleaved by the reagent to provide a cleaved second probe (ie., duplex 5 taught by Goodman *et al.,* in Figure 2) as recited in claim 35. Since Goodman *et al.,* teach repeating steps (b)-(e) (see claim 18, column 30 and Figures 1-4), the cleaved fragments taught by Goodman *et al.,* are detected by their fluorescent signals (see column 19, second paragraph), the cleaved fragments taught by Goodman *et al.,* substantially increases by thermal cycling of the reaction (see columns 25 and Tables III and IV in columns 26 and 28), and the presence of the cleaved fragments indicates the presence of the polynucleotide analyte in the sample (see column 19, second paragraph), Goodman *et al.,* must disclose detecting the accumulation of the cleaved second probe and determining whether the cleaved second probe accumulates exponentially over time (ie., from nothing to exponential amounts shown in Tables III and IV in columns 26 and 28), wherein said exponential accumulation of over time is indicative of the presence of said

target nucleic acid as recited in steps b) and c) of claim 35 and said detecting accumulation of the cleaved second probe comprising detection of fluorescence or phosphorescence as recited in claim 47.

Regarding claims 62, 63, 71, and 72, since Goodman *et al.,* teach forming in the presence of nucleoside triphosphates and template-dependent polynucleotide polymerase an extension of a target polynucleotide sequence hybridized with a binding polynucleotide sequence of a single stranded pattern polynucleotide comprising said binding polynucleotide sequence and two or more copies of a template sequence each containing one or more site specific cleavage sequences and cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences, cleaving into fragments said extension at cleavable polynucleotide sequences in the presence of means for specifically cleaving said cleavable polynucleotide sequences when said extension is hybridized with said site specific cleavage sequences, dissociating said fragments wherein said fragments comprise said primary polynucleotide sequence, hybridizing said fragments with said single stranded pattern polynucleotide, forming in the presence of said nucleoside triphosphates and said template dependent polynucleotide polymerase an extension of said fragments hybridized with said single stranded pattern polynucleotide, and repeating steps (b)-(e) above wherein steps (b)-(e) are conducted simultaneously or wholly or partially sequentially (see claim 18, column 30 and Figures 1-4) wherein said fragments are labeled with a fluorescence after cleavage (see claims 11-17 in claims 29 and 30, columns 14 and 15, and Figure 2), Goodman *et al.,* disclose incubating a sample with a cleavage agent under conditions wherein a first cleavage structure is

formed, said first cleavage structure comprising: i) a target nucleic acid (ie., target polynucleotide sequence taught by Goodman *et al.,*), said target nucleic acid comprising a first region and a second region, said second region upstream of and contiguous to said first region; ii) a first nucleic acid molecule comprising a first portion that is completely complementary the second region of the target nucleic acid (i.e., one site specific cleavage sequence); iii) a second nucleic acid molecule comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said first region of said target nucleic acid (i.e., another site specific cleavage sequence such as the primary polynucleotide sequence 2 in Figure 1); wherein said 5' portion of said second nucleic acid molecule is annealed to said first region of said target nucleic acid and wherein at least a portion of said first nucleic acid molecule is annealed to said second region of said target nucleic acid; cleaving said first cleavage structure with a cleavage agent so as to generate non-target cleavage product (ie., duplex fragment 5 in Figure 1) under conditions wherein a second cleavage structure is formed, said second cleavage structure comprising: i) said non-target cleavage product and ii) a probe oligonucleotide (ie., repeating template 1a in Figure 1) as recited in steps a) and b) of claim 62 wherein said 3' portion of said second nucleic acid molecule (i.e., 3' of another site specific cleavage sequence such as 3' of the primary polynucleotide sequence 2 in Figure 1) consists of a single nucleotide and said single nucleotide is complementary to said target nucleic acid as recited in claims 71 and 72. Since Goodman *et al.,* teach repeating steps (b)-(e) (see claim 18, column 30 and Figures 1-4), the cleaved fragments taught by Goodman *et al.,* are detected by their fluorescent signals (see column 19, second paragraph), and the cleaved fragments taught by Goodman *et al.,* substantially increases by thermal cycling of the reaction (see columns 25 and Tables III and IV

in columns 26 and 28), and the presence of the cleaved fragments indicates that the presence of the polynucleotide analyte in the sample (see column 19, second paragraph), Goodman *et al.,* must disclose cleaving said second cleavage structure with a cleavage agent so as to generate a cleaved probe, wherein said cleaved probe accumulates at an exponential rate over time (ie., from nothing to exponential amounts shown in Tables III and IV in columns 26 and 28), and wherein the accumulation of said cleaved probe at an exponential rate over time indicates the presence of said target nucleic acid in said sample and detecting said cleaved probe at a plurality of timepoints (see exponential amounts shown in Tables III and IV in columns 26 and 28) as recited in steps c) and d) of claim 62 and said detecting accumulation of the cleaved second probe comprising detection of fluorescence or phosphorescence as recited in claim 63.

Regarding claim 66, Goodman *et al.,* teach that said detecting said cleaved probe comprises detection selected from the group consisting of detection of radioactivity, luminescence, phosphorescence, fluorescence polarization, and charge (see column 19, second paragraph).

Therefore, Goodman *et al.,* teach all limitations recited in claims 35, 47, 62, 63, 66, 71, and 72

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman *et al.,* as applied to claims 35, 47, 62, 63, 66, 71, and 72 above, and further in view of Walker *et al.,* (US Patent No. 5,270,184, published on December 14, 1993).

The teachings of Goodman *et al.,* have been summarized previously, *supra.*

Goodman *et al.,* do not disclose that said detecting said cleaved probe comprises detection of fluorescence energy transfer as recited in claim 65.

Walker *et al.,* teach that a nucleic acid is detected using different methods such as detecting by fluorescence energy transfer (see column 12, last paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 65 wherein said detecting said cleaved probe comprises detection of fluorescence energy transfer in view of the patents of Goodman *et al.,* and Walker *et al.*. One having ordinary skill in the art would have been motivated to do so because the simple substitution of one kind of detection method (ie., the method taught by Goodman *et al.,*) from another kind of detection method (ie., fluorescence energy transfer taught by walker *et al.,*) during the process of detecting a cleaved probe, in the

absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made since the detection method taught by Goodman *et al.,* and the detection method taught by walker *et al.,* are used for the same purpose and are exchangeable (see column 12, last paragraph).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

12. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman *et al.,* as applied to claims 35, 47, 62, 63, 66, 71, and 72 above, and further in view of Mullis *et al.,* (US Patent No. 4,683,195, published on July 28, 1987).

The teachings of Goodman *et al.,* have been summarized previously, *supra.*

Goodman *et al.,* do not disclose that said first nucleic acid molecule is in concentration excess compared to said target nucleic acid as recited in claim 73. However, since the first nucleic acid molecule taught by Goodman *et al.,* contains multiple identical molecules, Goodman *et al.,* teach to provide a plurality of said first nucleic acid molecule as recited in claim 73.

Mullis *et al.,* teach that the amount of primer added is generally be in molar excess over the amount of complementary strand (template) in an amplification reaction in order to improve the efficiency of the amplification reaction (see column 7, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 73 wherein said first nucleic acid molecule is in concentration excess compared to said target nucleic acid in view of the patents of Goodman *et al.,* and Mullis *et al.*. One having ordinary skill in the art would have been motivated to do so because said first nucleic acid molecule taught by Goodman *et al.,* is served as a primer in the reaction (see claim 18 in column 30) and Mullis *et al.,* suggests that the amount of primer added is generally be in molar excess over the amount of complementary strand (template) in an amplification reaction in order to improve the efficiency of the amplification reaction (see column 7, second paragraph). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the method recited in claim 73 using said first nucleic acid molecule that is in concentration excess compared to said target nucleic acid.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,458,535 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are not identical to claims 1-27 of U.S. Patent No. 6,458,535 B1, claims 1-27 of U.S. Patent No. 6,458,535 B1 are directed to the same subject matter and fall entirely within the scope of claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application because: (1) the content of U.S. Patent No. 6,458,535 B1 indicates that a cleaved probe accumulates exponentially over time as recited in step c) of claim 35 and steps c) and d) of claim 62 (see column 73, lines 21-25); (2) the content of U.S. Patent No. 6,458,535 B1 indicates that the first nucleic acid molecule is in concentration excess compared to said target nucleic acid (see Example 17 in column 114, first

paragraph); and (3) the content of U.S. Patent No. 6,458,535 B1 indicates that a structure specific nuclease is a 5' nuclease such as FEN-1 from *Methanococcus jannaschii* (see column 10, fourth paragraph and column 18). In other words, claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are anticipated by claims 1-27 of U.S. Patent No. 6,458,535 B1.

15. Claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 5,994,069. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Although claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are not identical to claims 1-34 of U.S. Patent No. 5,994,069, claims 1-34 of U.S. Patent No. 5,994,069 are directed to the same subject matter and fall entirely within the scope of claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application because: (1) the content of U.S. Patent No. 5,994,069 indicates that a cleaved probe accumulates exponentially over time as recited in step c) of claim 35 and steps c) and d) of claim 62 (see column 73, lines 23-28); (2) the content of U.S. Patent No. 5,994,069 indicates that the first nucleic acid molecule is in concentration excess

compared to said target nucleic acid (see Example 17 in column 114, first paragraph); and (3) the content of U.S. Patent No. 5,994,069 indicates that a structure specific nuclease is a 5' nuclease such as FEN-1 from *Methanococcus jannaschii* (see column 10, fourth paragraph and column 18). In other words, claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are anticipated by claims 1-34 of U.S. Patent No. 5,994,069.

16. Claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,913,881 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Although claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are not identical to claims 1-5 of U.S. Patent No. 6,913,881 B1, claims 1-5 of U.S. Patent No. 6,913,881 B1 are directed to the same subject matter and fall entirely within the scope of claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application because the content of U.S. Patent No. 6,913,881 B1 indicates that a cleaved probe accumulates exponentially over time as recited in step c) of claim 35 and steps c) and d) of claim 62 (see column 71); (2) the content of U.S. Patent No. 6,913,881 B1 indicates that the first nucleic acid molecule is in concentration excess

compared to said target nucleic acid (see Example 17 in column 138); (3) the content of U.S. Patent No. 6,913,881 B1 indicates that a structure specific nuclease is a 5' nuclease such as FEN-1 from *Methanococcus jannaschii* (see column 16); and (4) the content of U.S. Patent No. 6,913,881 B1 indicates that the different detection methods that are claimed in claims 63, 65, and 66 (see column 8). In other words, claims 35, 47, 62, 63, 65-68, 71-73, and 78-84 in this instant application are anticipated by claims 1-5 of U.S. Patent No. 6,913,881 B1.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. No claim is allowed.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

June 8, 2006

FRANK LU
PRIMARY EXAMINER